UNIVERSITY OF MINNESOTA
SEP 11 19
LIBRARY

VOLUME XV APRIL 1959 NUMBER 4

Clinical Proceedings

OF THE CHILDREN'S HOSPITAL

WASHINGTON, D. C.

SYMPOSIUM: A SURVEY OF GROWTH FAILURE IN PEDIATRICS

INTRODUCTORY REMARKS
Captain T. E. Cone, Jr., M.C., U.S.N. 75
AN OUTLINE OF THE CAUSES OF GROWTH FAILURE
Commander C. L. Waite, M.C., U.S.N. 77
GROWTH FAILURE DUE TO MALNUTRITION
Lieutenant J. C. Parke, M.C., U.S.N. 84
GROWTH FAILURE ASSOCIATED WITH CONGENITAL HEART DISEASE
Lieutenant J. H. Mazur, M.C., U.S.N. 87
GROWTH FAILURE ASSOCIATED WITH RENAL DISEASE
Lieutenant K. W. Sell, M.C., U.S.N. 92
THE ROLE OF INFECTION IN GROWTH FAILURE
Lieutenant R. Miller, Jr., M.C., U.S.N. 96
CLOSING COMMENTS
Captain Cone 97
THE EDITOR'S COLUMN: TEAMWORK 99

Sobee® *formula was selected...*

Robert... *age 4 months*

Bobbie was a first child, and his mother didn't know what to do when he became a "crying baby," shortly after coming home from the hospital. He cried between feedings, and even *during* feedings. Then his doctor suggested a 2 day trial of Sobee... and the crying stopped! Now you've never seen such a bright, *cheerful* baby.

Willa... *age 5 months*

Like all allergic babies (like all *babies*), Willa needs love and lots of it. Willa gets love, in full measure, from her parents—while Sobee keeps her happily nourished.

Thomas... *age 7 months*

Tommy at 1 month was a colicky baby, irritable, usually crying—but physically normal except for an all-over rash. When Sobee replaced Tommy's milk formula, the crying stopped. His skin improved in a few days, and the rash was completely gone in a few more. Tommy liked Sobee, grew well on it. About a month ago Tommy was "weaned" back to milk, uneventfully.

SOBEE® (HYPOALLERGENIC SOYA FORMULA, MEAD JOHNSON) LIQUID/POWDER

Mead Johnson
Symbol of service in medicine

FP24308

MEAD JOHNSON & COMPANY, 422 Eig Building, 8641 Colesville Road, Silver Spring, Maryland, JUniper 91-222

CLINICAL PROCEEDINGS
OF THE CHILDREN'S HOSPITAL
2125 13th Street, N. W. Washington 9, D. C.

EDITOR-IN-CHIEF

J. William Oberman, M.D.

EXECUTIVE EDITOR

Gordon Loud

GENERAL MANAGER

Robert V. Morin

EDITORIAL BOARD

Robert H. Parrott, M.D.
Frederic G. Burke, M.D.
Joseph M. LoPresti, M.D.
E. Clarence Rice, M.D.
Sydney Ross, M.D.

MANAGING EDITORS

George J. Cohen, M.D.
Milton S. Glatt, M.D.
Grace H. Guin, M.D.

ASSOCIATE EDITORS

John Bayly, M.D.
Leonard B. Berman, M.D.
Stanley L. Blumenthal, M.D.
Winston E. Cochran, M.D.
Dan Feriozi, M.D.
Max Fischer, M.D.
Sanford Leiken, M.D.
Marvin I. Mones, M.D.
Marshall M. Parks, M.D.
George William Ware, M.D.
Ralph D. Whitley, M.D.

THE RESIDENT STAFF: Theodore H. Anders, M.D., Salvatore Battiata, M.D., Victor S. Cipolla, M.D., John J. Crotty, M.D., Timothy H. Daly, M.D., Mary Z. Daugela, M.D., Donald W. Delaney, M.D., George C. Emmanouilides, M.D., Joseph C. Evers, M.D., Spencer Frankl, M.D., D.D.S., Doris Gibbons, M.D., Loretta K. Gilmore, M.D., Seymour Z. Goldblatt, M.D., Nicholas P. Haritos, M.D., Wellington Hung, M.D., Iradj Mahdavi, M.D., Donald F. McGavisk, M.D., Albert Moniz, M.D., Richard D. O'Leary, D.D.S., Jose R. Puig, M.D., William N. Sterling, M.D., John Tkacz, M.D., Donald W. Wiczer, M.D., Hans-Joachim Wigger, M.D., and Nicholas Zouras, M.D.

RESEARCH FELLOWS: Gloria D. Eng, M.D., Christine W. Kehne, M.D., Hyun-Wha Kim (Oh), M.D., Frances Litrenta, M.D., William R. O'Reilly, M.D., Belinda C. Straight, M.D., Leticia U. Tina, M.D., and Sidney Lee Werkman, M.D.

PUBLICATIONS COMMITTEE OF THE MEDICAL STAFF: Robert H. Parrott, M.D., *Chairman*, Frederic G. Burke, M.D., Preston A. McLendon, M.D., E. Clarence Rice, M.D., Sydney Ross, M.D., J. William Oberman, M.D., and George William Ware, M.D.

PUBLISHED MONTHLY BY THE STAFF AND RESEARCH FOUNDATION OF THE CHILDREN'S HOSPITAL, WASHINGTON, D. C.

Cases are selected from the weekly conferences held each Friday at 12:30 P.M., from the Clinicopathological conferences and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $3.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.." The Children's Hospital, Washington, D.C. Please notify on change of address.

Copyright 1959, Children's Hospital

Second-class postage paid at Washington, D.C.

SYMPOSIUM:

A SURVEY OF GROWTH FAILURE IN PEDIATRICS*

Introductory Remarks

CAPTAIN T. E. CONE, JR., MC, U.S.N.†

The problem of growth failure is encountered by all of us, general practitioners and pediatricians alike, almost as a daily affair. At the U. S. Naval Hospital, we actually admit well over 100 children each year with a chief complaint of growth failure. A much larger group, however, are the purported growth failures in which someone feels that a particular child is too short, too tall, too thin or too fat. In our roles as physician-advisor and educator we can perform the maximum service to both parent and patient by first determining if there is a real basis for the parental anxiety, and if none exists explain why it does not. Several medical articles in the past few years have emphasized this one fact, that more than one-half the children whom the average pediatrician sees because of a complaint of growth failure have really nothing wrong with them. Actually, the percentage of normal children is probably much higher.

The first measurements of growth and development of which we have knowledge were done by a French count by the name of de Montbeillard who measured his son from the time of his birth in 1759 until 1777.[1] His figures were as accurate as any and can be matched with present-day figures. It was not too long ago that growth itself was considered to be something that one did not worry too much about and took for granted. The first accurate weight of a newborn infant was not recorded until about 1770 when Dr. Joseph Clarke presented a paper at the Royal Society meeting in London.[2] In the reports prior to this period, newborn infants were supposed to weigh one stone (14 pounds). We have come a long way in developing standards of reference since then.

How do we decide whether a child has a growth abnormality or not? Basically, we do it the same way the parents do, by some form of comparison. The parents compare the child with siblings of different age or sex or with neighbors' children. The physician, on the other hand, has several

* Presented by the Department of Pediatrics, U. S. Naval Hospital, Bethesda, Maryland, at The Metropolitan Area Pediatric Conference, February 27, 1958.

† Chief, Department of Pediatrics, U. S. Naval Hospital, Bethesda, Maryland.

means of comparing the child to other children on a more scientific basis. The so-called average height or weight for a particular age is not one of them because these are fixed values for the parents to compare their child against, and it may be only a lucky coincidence that the child's height or weight will match the average figure. Far better is the so-called percentile chart which is derived from the normal distribution bell-shaped curve. All the growth charts are based on this distribution; the mean is the fiftieth percentile; plus two standard deviations of the mean would include the ninety-seventh child; minus two standard deviation would include the third child. Therefore, in any measurement of height, for example, in 100 children routinely or randomly selected and arranged from the smallest to the tallest, purely by statistical reasoning, all of the children from number 3 to number 97 would be within the normal range of distribution for height and would be considered normal. Difficulty in the past arose from using a mean figure, and parents, of course, developed a great deal of anxiety because their child might or might not have met that particular figure. In the Wetzel grid and all the various grids commonly used in pediatrics the percentile channels of growth are developed and the patient's age is plotted against weight or height. In using these growth charts it is obvious that there is a wide spread between the children whose weight or height is low normal and those children in whom weight and height is high normal. Another important fact to remember is that when using these grids as standards of reference, it will be found that most normal children as they grow older will remain within their own growth channel.

McIntosh[3] writes that growth is a characteristic of the young of every species, so much so that we, whose attention is occupied with infants and children, find it all too easy to take growth for granted. The natural expectation that a young person will continue to increase in stature and weight and to advance at the same time in maturity is fulfilled so often in the face of a variety of every day vicissitudes that one too often believes that growth will take care of itself. All that is required, however, to prick this complacent bubble is to ask oneself whether a given infant or child is growing as well as he can and as he should. Here we come squarely up against the formidable pair of questions. How does one determine optimal growth, and how can it be attained? At the onset, it must be admitted that we have no way of knowing what is best in the matter of growth. We can establish that one way of growth is faster than another; admitting the risk of a *non sequitur*, we may even assert that since a new achievement in growth is demonstrably faster, it is therefore better. This is an attractive assumption in this period of plenty, but one that would be difficult to prove. Parents look fondly on the big car, and the big TV screen. Why not the big baby? Does not bigness give status, the feeling of success?

The clinician appreciates that in the immature animal growth is in some

degree a measure of health. In so saying, he seeks a healthy population in which to attempt a quantitative definition of satisfactory exemplary growth, and in so doing, he comes up at once against the related question of what is health, or specifically, who is healthy? It is all very well for the World Health Organization to define health as the absence of disease, but the identification of the truly healthy child in objective as well as in positive terms becomes a formidable task. One is usually willing to settle for the answer that the healthy child is a child who is growing properly. The crux of the problem rests with the definition of normal. The most important thing learned by pediatricians is that there are wide variations for almost any measurable phenomenon.

In the typical distribution bell-shaped curve, as previously mentioned, the mean plus and minus two standard deviations generally cover the biologic measurement from the third to the ninety-seventh of 100 random samplings. All measurements included within these two limits are generally considered statistically within the normal range. These can be projected onto Wetzel grids or onto the Stevenson charts, or any of the so-called "growth charts." Some investigators have included growth failure below the tenth percentile while others include growth failure below the third percentile. The crux of the matter is: Where do we cut off an observation from being normal? Is it not true that the great mass of pediatric practice which we consider abnormal may possibly be perfectly normal and exist between the normal plus or minus two standard deviations? Is there undue concern about normal variances, either anatomic or physiologic? I feel that the vast majority of children who are brought to us because of failure to grow fall within the normal range, the so-called nonmorbid normal variation.

REFERENCES

1. Scammon, R. E.: The first seriatim study of human growth, Am. J. Phys. Anthropol. **10:** 329, 1927.
2. Clarke, J.: Observation on some causes of the excess of mortality of males above that of females, Phil. Trans. Roy. Soc., London, **16:** 122, 1786.
3. McIntosh, R.: On growth and development, Arch. Dis. Childhood. **32:** 261, 1957.

An Outline of the Causes of Growth Failure

Commander C. L. Waite, MC, U.S.N.

Growth failure is such a common and universal problem that there is no difficulty in finding an outline of its causes. All the standard pediatric textbooks have an excellent outline up to a point. The difficulty is in finding one

Conditions Characterized by Impairment of Growth (Impaired statural growth)	Conditions Characterized by Acceleration of Growth (Accelerated statural growth)	Conditions Characterized by Distortion of Growth (Anomalous or distorting morphological growth)
1. Nonmorbid normal variations	1. Nonmorbid normal variation	1. Obesity a. Dietary b. Froelich's (hypothalamic) c. Adrenal (Cushing's) d. Laurence-Moon-Biedl
2. Hypopituitary dwarfism	2. Pituitary gigantism	2. The Chondrodystrophies a. Achondroplasia b. Dysostosis multiplex c. Osteochondrodystrophy d. Chondrodysplasia
3. Primordial dwarfism	3. Primordial gigantism	3. Morphological anomalies of embryonic origin in which no new anomalies appear during the growth period, e.g. arachnodactyly, mongolism.
4. Progeric dwarfism	4. Eunuchoid gigantism	4. Impairments of bone or neuromuscular function secondary to disease or trauma during growth period (e.g. rickets, osteochondroses, tuberculosis, poliomyelitis, hyperparathyroidism, etc.)
5. Stunted growth of metabolic or nutritional etiology: a. Hypothyroidism b. Celiac disease (malabsorption syndrome) c. Cystic fibrosis of the pancreas (mucoviscidosis) d. Chronic renal disease e. Chronic liver disease f. Simple malnutrition (starvation) g. Aganglionic megacolon h. Inborn errors of metabolism i. Congenital heart disease j. Chronic pulmonary disease k. Psychogenic causes l. Chronic infections (?) m. Stunted growth associated with gonadal dysgenesis and adrenal hyperplasia.	5. Hyperthyroidism	5. Ectodermal dysplasia, dental anomalies.

FIG. 1. An outline of growth failure[3-6]

that covers the majority of the causes, groups them in some semblance of order and places them in proper relationship to one another. Figure 1 is our attempt at such an outline, but even it is not complete since it does not show the physiological relationships. A complete outline of growth failure should include sexual precocity and failure to reach sexual maturation. However, this is almost another subject in itself. It is not surprising that a list of factors and disease processes influencing growth resembles an index of a text on the entire field of pediatrics. It will be noted in figure 1 that growth failure implies things other than being small for one's age. Being greatly oversized is equally as much a tragedy as being small, as any six

foot teen-age girl will tell you. Similarly, any condition resulting in distorted body growth must be considered as a type of growth failure, one of distorted pattern rather than of distorted size. If there are any shortcomings in this outline, it is a lack of completeness in failing to consider all the known causes of growth failure. Furthermore, the frequent overlap of the multiple causes operative in any disease process is not shown. For example, in cystic fibrosis of the pancreas, various factors operate, such as malabsorption of ingested food, chronic respiratory disease, frequent infections, and altered electrolyte balance.

In this outline the most commonly encountered causes of growth failure are found in the left hand column under conditions resulting in impaired statural growth. In that group, those conditions included in item 5, stunted growth of metabolic or nutritional etiology, are the few causes of growth failure that are totally or partially amenable to treatment: hypothyroidism, celiac disease, cystic fibrosis of the pancreas, some renal disease, malnutrition, aganglionic megacolon, some inborn errors of metabolism, those congenital heart diseases amenable to surgery, psychogenic causes, infections, and those due to the adrenogenital syndrome. Unfortunately, at the present time, most of the other categories assume the role of medical curiosities or museum pieces about which little or nothing can be done by the physician except to give them a name and describe them.

Generally, the term dwarfism is taken to mean those types of growth failure characterized chiefly by impaired statural growth. Talbot[1] has defined the term more specifically to designate any child shorter than 90 per cent of other children of the same chronological age living in the patient's community. I personally do not care for this particular definition because the obvious assumption is that 10 per cent of the children in the neighborhood are dwarfs. Most physicians actually reserve the term dwarf to describe children falling below the third percentile of normal.

The best definition of primordial dwarf is probably that of Lawson Wilkins[2] who defines this type of dwarf as being synonymous with the genetic or constitutional dwarf; a dwarf in whom there is no retardation of the developmental processes or other evidences of endocrine deficiency. Such dwarfing may indeed be genetically transmitted, as shown by certain tribes of aboriginal pygmies. In other races, it may also be hereditary and transmitted through normal as well as dwarfed members of a family. More frequently, however, it occurs in normal families as isolated sporadic instances, the etiology of which is not understood.

The nonmorbid normal variations of impaired statural growth are extremely common and include all the children brought to physicians by mothers who think that such a child might be small for his age when compared to the child next door. Some of these children are somewhat small for

their age but the physician who does a careful examination and performs a careful search for underlying diseases will usually be able to assure the mother that her child is destined to remain at the lower limit of normal in the typical distribution curve.

Hypopituitary dwarfism (Lorain-Levi) is an extremely rare type of dwarfism; the exact etiology is not known, but some malfunction of the pituitary is suspected. Very rarely one can demonstrate a tumor or other destructive lesion of the pituitary gland. It is very difficult to make an early clinical diagnosis of this type of dwarf, and, in the absence of localized pituitary signs, proof depends on finding impairment of the gonadotrophic, thyrotrophic, or adrenotrophic functions of the pituitary. When a dwarf remains sexually infantile well into adult life, it is safe to assume there is some deficiency of both growth and gonadotrophic hormones of the pituitary. Urinary excretion of both the follicular-stimulating hormone and the 17-ketosteroids are low. Pituitary dwarfs usually appear normal at birth and grow at a normal rate for the first few years. This implies some factor other than the lack of pituitary hormone; perhaps there is some inborn genetic drive in the cell that is lost in reaching adulthood. Around the age of 4 or 5 years, stunting usually becomes apparent. There is a marked delay in the osseous development with the epiphyses remaining open almost indefinitely; this is a paradox since, normally, as long as the epiphyses remain open the child keeps on growing. Older pituitary dwarfs retain their childish features but develop age lines most prominent about the eyes and mouth due to the loss of tissue elasticity with age. These are the dwarfs one sees in the circus.

The progeric (Hutchinson-Gilford) dwarf is very rare but so bizarre that it would be difficult to misdiagnose one. The most striking features are premature senility, arteriosclerosis, early closure of the epiphyses, a characteristic facial appearance, alopecia, absent ear lobes, and an underdeveloped jaw. These patients have many of the features of ectodermal dysplasia, i.e., sparse hair, underdeveloped teeth, etc., so that it is very difficult to differentiate these syndromes in their early stages. These children usually die in the second decade of life. The serum lipoprotein level in an 11 year old progeric dwarf was recently found to be very high, whereas the total body fat was quite low. This might symbolize some disturbance of lipid metabolism and perhaps this disease will eventually fit into the group of diseases of inborn errors of metabolism.

Hypothyroidism, particularly the congenital athyreotic type, should be very hard to misdiagnose as a cause of growth failure, and yet diagnosis is frequently needlessly delayed. The derivation of the word cretin is quite interesting. It is said that cretin comes from the French, *chrétien*, meaning Christian. The symbolism is that Christians weren't particularly stupid but

rather passive and were prone to turn the other cheek. While physical growth can be readily promoted in these children with the addition of adequate thyroid extract, the mental deficiency is not so responsive. In general, however, the earlier congenital hypothyroidism is diagnosed and treated, the better the end result.

We have recently observed 2 cases of Hirschprung's disease admitted to the hospital with a diagnosis of growth failure. One child was far below the third percentile in weight and demonstrated signs of marked undernutrition: potbelly, sallow complexion, thin legs, etc. Once we were able to observe him in the hospital and observe the alternating constipation and watery diarrhea, the diagnosis of congenital megacolon was confirmed. This child was operated on, and made a rapid return to a normal growth pattern. In this disease, some interference with normal intestinal absorption is postulated as the cause for growth failure.

Psychological causes of growth failure include anorexia nervosa associated with emotionally disturbed children, psychic vomiting and rumination.

Stunted growth associated with gonadal dysgenesis, properly called the Bonnevie-Ullrich-Turner syndrome, is not too uncommon. These patients were formerly considered to be females with undeveloped ovaries. Recently, however, tests using buccal smears and the examination of epithelial cells for chromosomal pattern have shown that the majority of these patients are chromosomal males. Features of this syndrome include webbing of the neck, eye muscle defects, lymphedema of the back of the hands and feet and coarctation of the aorta. The dwarfing in the Bonnevie-Ullrich-Turner syndrome is not marked. The maximum height attained is usually 52 to 58 inches; dwarfing is assumed to be due to a congenital defect linked to the other anomalies.

The problem in the adrenogenital syndrome, in addition to the sexual precocity, is an early rapid growth spurt with early fusion of the epiphyses. A child who went through the first eight or nine years of his life always bigger and more sexually developed than his peers enters adolescence well behind them due to the absence of a secondary growth spurt. The usual attained height is about 54 to 63 inches. Urinary excretion of 17-ketosteroids is elevated, and the determination of this substance is useful in diagnosing this condition. Some patients, in addition, lose excess salt in the urine, and others have hypertension. Early treatment with minimal amounts of adrenal corticosteroids will delay closure of the epiphyses and somewhat allay growth failure. A definite familial occurrence of this disease has been described by many authors.

The first condition to be considered in those characterized by accelerated statural growth is the nonmorbid normal variation, which is probably the most common type of accelerated statural growth. One patient recently ob-

served was aged 2 years; her height was more compatible with that of a 4 year old. A thorough search for pathologic deviations was negative. The bone age matched the height age; the body proportions were normal. Her father was 6 feet tall; her mother was 5 feet 6 inches.

The other causes of gigantism are extremely rare. Pituitary gigantism is due to hyperfunction of the eosinophilic cells of the anterior pituitary gland occurring before puberty. Growth is usually greatest at puberty; an occasional patient has signs of increased intracranial pressure accompanying a pituitary adenoma. Hereditary or primordial gigantism implies increased stature inherited from one or both parents or near relatives. Several tribes in Africa, notably the Watusi, bear witness to the hereditary aspect of this particular type. Eunuchoid gigantism is gigantism associated with gonadal dysfunction. These patients remain sexually immature despite their rapid growth and have a low urinary excretion of androgen or estrogen. Hyperthyroidism is a cause of gigantism. Children with increased thyroid function exhibit increased statural growth though not to the degree exhibited by the other types of gigantism. The secondary sexual characteristics are late in appearing. Even in normal individuals, there is always an interplay between the growth hormones and the sexual hormones. Generally children who mature sexually very early are much shorter than their chronological peers, and conversely, children who have a late onset of the secondary sexual characteristics usually grow a little taller.

Obesity is probably the most common condition characterized by the distortion of growth, and obesity of dietary origin is by far the most frequent. The underlying reasons for obesity, particularly in children, are sometimes obscure and fraught with psychiatric implications. The treatment of dietary obesity in the preadolescent is usually very difficult; it is not easy to get these children to stay on a diet or lose weight.

Less common causes of obesity include the so-called Froelich's syndrome. This diagnosis is frequently misapplied to big fat boys who, although they appear to have an unusually small penis, merely have so much fat that their genitalia are hidden. The true Froelich's syndrome is due to a hypothalamic lesion, and the obesity is not uniform but is concentrated on the trunk. These boys do have small genitalia, but in addition have retarded growth, papilledema and optic atrophy.

We are seeing more examples of Cushing-like disease or syndrome than we ever thought we would see a few years ago. True Cushing's disease was defined by Cushing in 1932 as due to a pituitary basophilic adenoma and was very rare indeed. Actually, in children such an adenoma is usually not found. In the younger children, adrenal tumor is the more common cause of the Cushing syndrome. However, the most common cause of a Cushing-like syndrome today is that due to the therapeutic use of adrenal steroids.

Another cause of obesity is the Laurence-Moon-Biedl syndrome. This is a rare cause of obesity and is inherited perhaps as a recessive trait. These patients have, along with their obesity, mental retardation, hypogenitalism, polydactylism, and retinitis pigmentosa. Prognosis in this particular syndrome is quite poor.

Included in the chondrodystrophies is classical achondroplasia, which is easily diagnosed. Children so afflicted usually have normal head and trunk proportions, but very short extremities. This disease can be readily diagnosed in the newborn. The face and body proportions are quite typical. Dysostosis multiplex (Hurler's disease, gargoylism, lipochondrodystrophy) is thought to be a congenital recessive hereditary defect characterized by grossly retarded cartilaginous growth of the vertebrae and of the long bones. Hepatosplenomegally, coarse facies (giving rise to the term gargoylism), a hunched over appearance (due to kyphosis), later-developing cloudy corneas and mental retardation are usually present to some degree.

Another type of chondrodystrophy is osteochondrodystrophy (Morquio's disease). This resembles dysostosis multiplex in several respects as far as the skeletal changes are concerned, but there is no associated hepatosplenomegaly, no corneal involvement, and usually no mental deficiency. Finally, there is a large group which can only be described as chondrodysplasias. This includes such diseases as ectodermal chondrodysplasia or the Ellis-Van Creveld syndrome. Components of this syndrome include ectodermal dysplasia, chondrodysplasia, polydactylism and some form of congenital heart disease. Albers-Schoenberg disease (osteopetrosis) and Ollier's disease (multiple enchondromatosis) also fit into this classification.

Morphological anomalies of embryonic origin in which no new anomalies appear during the growth period include localized growth failure, amelias (the lack of arms or legs), the hemimelias (absence of the proximal ends of the extremities) and the phocomelias. Arachnodactyly is another syndrome in which the growth pattern is set at birth and does not change.

Mongolism represents one of the more common forms of growth failure. This is a generalized growth failure, implying an embryonic origin, due probably to a severe insult to the fetus around the eighth week of gestation. The anomalies are characteristic but may occur in isolated form in normal children (simian line, Brushfield spots, and epicanthal folds). Probably the only constant finding in mongolism is mental deficiency. There may be an associated atrioventricularis communis or annular pancreas.

Ectodermal dysplasia and the dental anomalies form another interesting group. Some day we will be able to fit this disease into a category with some of the other diseases but right now they are in a class by themselves. There are many aspects of ectodermal dysplasia which resemble the Ellis-Van Creveld syndrome and there are many features of this disease that

resemble the progeric dwarf. Perhaps these three belong in the same category.

REFERENCES

1. Talbot, N. B.: Dwarfism in children, Bulletin of the New England Medical Center, **7**: 117, 1945.
2. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Illinois, Charles C Thomas, 1957, p. 161.
3. Hampson, J. L., and Money, J.: The Child with Disorders of Physical Growth: in H. Michal-Smith, ed.: Management of the Handicapped Child, New York, Grune and Stratton, 1957, p. 173.
4. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Illinois, Charles C Thomas, 1957, p. 120.
5. Stevenson, S. S.: Growth failure, Pediat. Clin. N. America. **1**: 433 (May), 1954.
6. Green, M., and Richmond, J. B.: Pediatric Diagnosis, Philadelphia, W. B. Saunders Company, 1954, pp. 205–208 and 263–273.

Growth Failure Due to Malnutrition

Lieutenant J. C. Parke, MC, U.S.N.

Nutritional deficiencies both in essential elements and in total calories are frequent causes of inadequate growth in children. We know that the infant and child must have food for growth and for maintenance and repair of body tissues, and we know that to supply the caloric requirement alone is not sufficient to promote optimal growth. Since there is no adequate definition for optimal growth there can be no optimal diet, and physicians no longer calculate the exact amount of calories, protein, carbohydrate and fat for an infant or child of a certain specific age. "Homeostatic mechanisms" are now relied upon and a child is allowed to take what the mechanisms demand. We therefore occasionally see a child whose homeostatic mechanisms have not been fulfilled for one reason or another and a precarious nutritional balance results. Further reduction of nutrients, or infections, diarrhea, etc., may upset this balance, and the stage is then set for further metabolic changes with resultant failure to grow.

Classification of malnutrition is probably best done etiologically and is best considered in two main divisions: primary, where the ingestion of food of adequate quality is insufficient, and secondary, where there is an adequate intake but defective assimilation. Among the primary causes of malnutrition are the so-called price rationing or economic factors, faulty dietary habits, and anorexia nervosa.

Failure to develop satisfactory eating habits is probably the most common reason for inadequate weight gain. Many children who have anorexia exhibit personality patterns with symptoms of irritability, hyperexcitability and tension. Such children are very difficult to bring to the table. They usually pick at their food, and are impatient to leave before completing the meal. Many appetite stimulants have been used to correct such anorexia. Good results have been reported by some using combinations of thiamin and vitamin B_{12} with reserpine and/or nembutal.

Under the secondary causes of malnutrition, the first to be considered is interference with digestion and absorption. The first one of this group is malnutrition due to deficient digestive secretions, fibrocystic disease of the pancreas probably being the most common in order of frequency. Other members of this group include malnutrition arising from steatorrhea, achlorhydria, or biliary duct atresia. The second large group in which there is interference with digestion or absorption includes those conditions causing too rapid passage of food through the gastrointestinal tract, or due to an altered gastrointestinal absorptive surface. Included in this group are rumination, esophageal stenosis, pyloric stenosis, massive resection of the intestinal tract, chronic diarrhea, and intestinal parasitism. There is no simple correlation between the presence of parasites in the gastrointestinal tract and malnutrition. The parasites which derive their nutrients from the host tissue by attaching themselves to the wall of the bowel probably play the greatest role, but, in such cases, precarious nutritional balance has already existed and the parasites act only as another insult which the body cannot tolerate and remain in nutritional balance. Host resistance and the number of parasites obviously are factors to be considered.

The second main group included in secondary causes of malnutrition is increased nutritional requirement without an increased intake of food. Causes would include tissue destruction occurring during febrile illness, environmental temperature changes and the administration of certain drugs. A third group of secondary causes is interference with utilization, which may be subdivided into two main groups: enzyme deficiencies, occurring in such diseases as diabetes mellitus, hypopituitarism, and hypothyroidism; and impaired oxygenation, occurring in congenital heart disease and in chronic pulmonary disease.

In simple starvation, or simple marasmus, the body weight of the child is about 75 per cent of the average for the child's age. The diet is deficient both in calories and in protein. The onset of the illness is insidious and is first manifested by a decrease in the expected weight gain for age. The child adapts to this inadequate food supply without apparent wasting. Another clinical form is the so-called sugar-baby kwashiorkor which is not often seen, since simple marasmus often progresses directly to the third type,

kwashiorkor, or malignant malnutrition. In the child with sugar-baby kwashiorkor, body weight is usually about 60 per cent of the average for the child's age. The subcutaneous fat of these children is retained and there is no marked muscle wasting. Here the diet is deficient in protein only. The calories are usually quite adequate, if not increased. This type is best treated by the administration of a high protein diet.

Marasmic kwashiorkor, or malignant malnutrition, is considered by the World Health Organization to be the third most common disease in the world. We do not see this condition in the United States but we do not know how often we prevent kwashiorkor by feeding children with simple starvation an adequate diet. Clinical features of marasmic kwashiorkor include retarded growth, mental symptoms including apathy and irritability, edema, hypoalbuminemia, skin dyspigmentation, and dermatoses.

In spite of the hypoalbuminemia, plasma proteins are normal or only slightly lowered. The plasma globulins, interesting to note, are always increased; this is particularly true of the gamma globulins and alpha globulins. Dyspigmentation and dermatoses are quite common; the origin of these has given rise to much controversy. The hair is usually fine, straight, bleached, and frequently has a reddish color. Skin lesions vary from a dry hyperchromic skin to a desquamation of the skin with erythematous and bleeding surfaces simulating pellagra. Gastrointestinal disorders are frequent. These include anorexia, vomiting, and attacks of diarrhea or steatorrhea-like stools alternating with constipation. Salmonella or Shigella organisms may be cultured in approximately 10 per cent of these cases. The anemia which is usually seen is slightly macrocytic although with secondary intestinal parasitism it may be microcytic, and in about 40 per cent of cases is noted to be normocytic. Hepatomegaly is found in approximately 6 per cent of cases; its origin is another source of controversy among the people in the areas where kwashiorkor is seen. There is decreased glucose tolerance and decreased intestinal amylase activity. Pathological changes in the liver include fatty infiltration, necrosis, and/or fibrosis; however, liver function tests are usually normal. Electrolyte disturbances are most characteristic and have been studied in detail. These include an increased extracellular volume of fluid and intracellular overhydration. Muscle and skin biopsies have shown an increase in the total content of water, sodium and chloride and a decreased amount of potassium. There is usually an excretion of a rather large volume of hypotonic urine. Mortality in this group is up to 80 per cent, if untreated.

How does malnutrition cause growth failure? First are causes which are related to intake of protein. Insufficient intake of protein forces tissue and plasma proteins to satisfy requirements for energy with resultant depletion of tissue mass. This is especially true when there are increased demands for

energy during an infection, or loss of calories through diarrheal stools. In addition, a decreased intake of protein interferes with endocrine function and tissue cells fail to survive. Pathologic changes are found in the adrenal and pituitary glands of malnourished individuals. Urinary excretion of 17-ketosteroids is low, and secretion of the gonadotrophic and thyrotrophic hormone is diminished.

Short periods of inadequate intake and secondary loss of electrolytes also limit the rate of anabolism of tissue, and secondarily inhibit important enzyme systems which causes embarrassment of cell function. An example is the dilution of the depleted potassium of the intracellular fluid seen in severe malnutrition with superimposed diarrhea and dehydration. The concentration of this cation falls below the level required for activation of the phosphate transfer enzyme system which catalizes the release of phosphate-bound energy which in turn is required for the transport of cations across the cell membrane; cell metabolism is impaired and the cell dies.

In summary, malnutrition must be regarded as an aggregate of syndromes of varying etiology but of single pathogenesis. The single pathogenesis is deficient cellular utilization of nutritional elements with consequent metabolic changes which are responsible for growth failure. Any interruption of the process, starting with the ingestion of food and ending with its utilization by the cell, may be responsible for the pathologic process.

Growth Failure Associated with Congenital Heart Disease

LIEUTENANT J. H. MAZUR, MC, U.S.N.

Congenital heart disease is, in our hospital, the second most common cause of growth failure, being surpassed only by the idiopathic type for which we can find no explanation. Growth failure resulting from congenital heart disease is common because congenital heart disease itself is so common, estimates ranging from 1 in 1,000 to 1 in 1,500 live births. Almost all of these manifest some degree of growth failure. It should be thought of as being closely correlated with the symptoms of exertional dyspnea, easy fatigability and exercise tolerance limitation in older children and adults.

The child under the age of 2 years does not normally demonstrate a great deal of activity. His motor system does not provide him with the facilities to ambulate, so that when he has an inadequate heart he manifests the

demand for an increased blood supply by failure to grow and develop, rather than by exertional dyspnea. The child with growth failure due to congenital heart disease is typically described as having a gracile habitus; i.e., he has a greater deviation from normal of his weight than height. These children are not tall but they appear to be somewhat taller than they actually are since they have rather slender arms and legs. This gracile habitus is described as being typical in atrial septal defects, but is seen in other forms of congenital heart disease as well, particularly when there is a left to right shunt. However, there are also numerous cases of congenital heart disease in which both height and weight seem to be proportionally decreased. Because growth is normally most rapid during the first two years of life, any condition causing deviation from normal growth is going to be most marked during this period.

Congenital heart disease is a difficult problem to diagnose and manage in the child under 2 years of age. Murmurs are not so helpful; the child is not exercising, he may not yet have become cyanotic and his pulmonary vasculature is in a state of change. Therefore, any information which could be gathered about the growth of these children would be of value; remarks during this discussion will be confined primarily to weight. Weight as a measure of growth is really not so satisfactory as is height but is probably more accurately determined in the child under 2 years of age.

Congenital heart disease is an important cause of growth failure not only because of its frequency, but also because, in the last decade or so, there has come to be a great deal which can be done for these children. Cardiovascular surgery has progressed to the point where one can often correct the basic underlying anatomic cause and restore both the cardiovascular system and the physical growth of the child to normal. It is becoming increasingly more important that these lesions be diagnosed early, their significance realized and an attempt made to correct them. Even in the child whose lesion is not at the present time amenable to surgical correction, a study of growth is a valuable index of cardiac function and reserve; this helps us in planning therapy and future management. Growth studies might not be quite so important in the 2 year old with congenital heart disease as they are in the 4 to 6 year old, but are of value in deciding when special studies which have an inherent risk are indicated, and when they can be safely delayed.

Because a study of growth in these children is so important, it should be recorded properly on a Wetzel grid or any of the standard growth charts wherein a child's height and weight may be recorded serially. A description of height and weight at each clinic visit noted on the chart means a great deal to the observer who must decide the necessity for operative correction.

The etiology of growth failure in congenital heart disease is a subject about which little is known. Taussig feels that anoxemia is probably the

important cause. In her classic monograph,[1] she states that the rate of growth and degree of development of the individual offer a clue to the severity of the cardiac anomaly. Growth is frequently stunted in the child who has persistent cyanosis and suffers a severe degree of anoxemia. The same is true, however, when there is a left to right shunt of such magnitude that the body lacks an adequate supply of oxygenated blood.

Growth failure is characteristic of nearly all children with cyanotic congenital heart disease but may actually not be very severe; a number of these children fall above the third percentile. In a reported series of 200 cases from England, it was felt that a rough correlation between the degree of cyanosis and growth failure existed; the more cyanotic, the greater the growth failure. When a comparison was made between those children with tetralogy of Fallot and those with other varieties of cyanotic congenital heart disease, it was found that in the presence of the same degree of cyanosis, growth failure was not so severe in the children with the tetralogy as it was in the other types.

A second suggested cause for growth failure is inadequate systemic blood flow. There are three sub-groups under this particular heading, all of which can cause an inadequate systemic blood flow. The first is an intracardiac block. In adults, this block is most commonly seen in mitral stenosis where there is an anatomical obstruction to the flow of blood. In congenital heart disease, stenosis of the aorta at the usual site of coarctation, or at the aortic valve, aortic infundibulum, pulmonary valve, pulmonary infundibulum, pulmonary artery or any location where there is a mechanical limitation to the amount of blood that can be put through the system all may produce inadequate cardiac output. Another fairly common cause of block is that due to a limiting membrane. The most common representative of this group, particularly under the age of 2, is endocardial fibroelastosis, where the endocardium is thick and unexpansible and cannot permit the heart to accumulate a satisfactory amount of blood for normal stroke volume. In some young children, myocarditis with a subsequent diffuse myocardial fibrosis may produce the same limiting membrane in the myocardium; in older children and adults, constrictive pericarditis may result in the same type of interference with systemic blood flow.

Another cause, and the most common one, of inadequate systemic blood flow in congenital heart disease is a left to right shunt. The heart pumps much larger volumes of blood than normal; from 50 to 80 per cent of circulating blood volume may be recirculated through the lungs.

A third cause of inadequate systemic blood flow is congestive heart failure. The heart failure most often observed in congenital heart disease is the so-called backward type of failure, and it may occur either in the circulatory blocks or the left to right shunts.

There is actually no real explanation for the mechanism whereby inade-

quate cardiac output or cyanosis produces growth failure. All that can be offered at the present time is a teleologic explanation. Tissues need oxygen, and whenever a defect is present which is characterized by cyanosis or in which there is anoxemia, or whenever the systemic blood flow is so inadequate that the volume of blood being received by an organ in a given period of time is inadequate, the organ may do one of two things, and usually does both. First, the tissue may extract more oxygen from the blood being presented to it, the arteriovenous oxygen difference increasing from 3–5 volumes per cent up to 6–7 volumes per cent; and second, the tissue may not grow normally, thereby decreasing its demand for oxygen.

Growth failure resulting from circulatory block or inadequate systemic blood flow is variable. Death may be produced in the neonatal period or the child may be minimally retarded in growth. All degrees of growth retardation exist between these two points. Growth failure is usually considered to be most marked in an atrial septal defect and in some cases of patent ductus arteriosus. It is reversible by surgery in many cases and therein lies the importance of recognizing its significance. Richards[2] studied a group of postoperative children who had Pott's procedures for repair of the tetralogy of Fallot, and another group who had ligation of a patent ductus arteriosus. Most of the children in whom the ductus was ligated showed moderate improvement in height and weight. Very few postoperative children with the tetralogy showed any significant improvement. Her explanation for this was that in repair of the tetralogies, one substituted a left to right shunt for the previous right to left shunt. Even though arterial saturation often increased up to 85 or 90 per cent—very close to normal levels—no significant change in the growth curve occurred. This production of a left to right shunt may not be as important as Richards felt. Her cases were operated on between 1946 and 1949 and, at that particular time, only children who were rather severely involved were being operated on.

Another potential cause of growth failure in congenital heart disease is genetic linkage. Nadas[3] feels that this is a significant cause. Congenital heart disease may well be associated with growth failure as either a genetically linked defect, or the two defects may be associated with the same teratogenic agents. In 75 children with congenital heart disease seen at the Naval Hospital in the last 18 months, there was an incidence of associated defects of about 33 per cent, much higher than one would find in any group of 75 normal children. Abnormalities included prematurity, mental retardation, craniostenosis, epilepsy, cleft palate and hare lip, cretinism, mongolism, club feet, and laryngeal stridor. Another factor illustrating the role that genetic linkage may play is the sex difference occurring in congenital heart disease. Patent ductus arteriosus and atrial septal defect are most commonly seen in girls, and coarctation of the aorta and aortic stenosis are

most commonly seen in boys. Such sex linkage may also play a role in the etiology of the growth failure. Other evidence of this linked genetic defect often advanced is the fact that some well known syndromes exist in which congenital heart disease is associated with disturbance of growth: mongolism, Gregg-Swann syndrome, Turner's syndrome, Marfan's syndrome and Marchesani's syndrome.

Respiratory infections have long been recognized as important causes of growth failure in children with left to right shunts. Usually, the more severe the shunt, the more severe the respiratory infections and the more severe the growth failure. In the last decade or so since fairly adequate chemotherapy and chemoprophylaxis for infection have been available, this factor has become more apparent. Many children show rather marked improvement when infection is properly managed.

A fifth cause for growth failure is congestive heart failure and its resultant anorexia. Balance studies have not been done in these young children; most investigators' experience is that caloric intake appears to be rather poor. The explanation for this is not known. Anorexia is characteristic of congestive heart failure in older children and adults. This may be related to dyspnea in the young child, difficulty in feeding, or bowel congestion due to chronic passive congestion in the liver and viscera. The use of diuretics and salt restriction over a long period of time may well produce electrolyte disturbances which may interfere with appetite and thereby interfere with growth. Of course, congestive heart failure *per se* is a cause of an inadequate systemic blood flow, as previously described.

Most of the recent work in the last few years has been in children with patent ductus arteriosus. This lesion has been fairly well defined for a number of years, surgical repair has been in use for 13 or 14 years, thousands of these children have been operated on all over the country, and there is a great deal of long term follow-up clinical material available for study. Recently, Engle and associates[4] reported that 40 per cent of children with patent ductus arteriosus who were operated on at age 4 or 5 years had moderate to severe growth failure. They did not do nearly as well as expected postoperatively, and Engle's group makes the plea that one should follow these children very closely from the time when their lesion is first diagnosed. They believe that operation is indicated within a few months of onset of a change in the slope of a growth curve. This frequently will be necessary within the first three years of life, and surgery has now progressed to the point where the operation in the hands of a competent cardiac surgeon is easily performed with very low risk even on the youngest child. This reiterates that mild to moderate growth failure alone, in children with patent ductus arteriosus, atrial septal defect, pulmonic stenosis, coarctation of the aorta, or any other lesion which becomes amenable to low risk

surgery, is probably a fairly good indication for operation. In the more complicated defects, such as ventricular septal defect, tetralogy of Fallot, etc., where the operative risk is somewhat higher, growth failure, while not to be considered alone as an indication for surgery, should play a major role in determining the optimum time for surgery.

REFERENCES

1. Taussig, Helen B.: Congenital Malformations of the Heart, New York, Commonwealth Fund, 1947.
2. Richards, M. R.: Pre and postoperative growth patterns in congenital heart disease as shown by the Wetzel grid, Pediatrics **9:** 77, 1952.
3. Nadas, A. S.: Pediatric Cardiology, Philadelphia, W. B. Saunders Company, 1957.
4. Engle, M. A., Holswade, G. R., Goldberg, H. P., and Glenn, F.: Present problem pertaining to patency of the ductus arteriosus; I. Persistence of growth retardation after successful surgery, Pediatrics **21:** 70, 1958.

Growth Failure Associated with Renal Disease

Lieutenant K. W. Sell, MC, U.S.N.

Although chronic renal disease is well known as one of the most frequent causes of growth retardation in children, details of the nature of the dependence of normal growth on kidney function are very poorly understood. All pediatric texts in their discussion of growth retardation refer to the complications of renal rickets, but growth failure in the absence of rickets is only cursorily mentioned.

In an attempt to elucidate the causal relationship of various renal functions to growth failure, West and Smith[1] reviewed the clinical records of some 41 patients with chronic renal failure. The first point of interest was that about one half of these patients demonstrated height or weight values above the tenth percentile, therefore falling into the normal range. He stated that chronic infection in the absence of significant obstruction, or chronic unilateral renal disease with obstruction resulted in no long term growth effect. All cases noted to fall below the tenth percentile had severe bilateral involvement; either this was manifested by a primary defect of the kidneys as exemplified by renal hypoplasia, or severe bilateral obstructive phenomena with superimposed infection. Study of female patients admitted to our hospital during the past two years who were discharged with a diagnosis of pyelonephritis revealed that even in those patients who have

severe enough disease to require nephrectomy, all with the exception of one were above the tenth percentile in height and weight. It is interesting to note that the one exception occurred in a 10 year old who actually had just one episode of acute pyelonephritis; the growth failure was probably unrelated.

It is very probable that the decreased food intake in patients with chronic renal disease (partially explained by their need to ingest large quantities of water, leaving little time or gastric space available for food intake) accounts for much of the stunting of growth seen in kidney disease. Other causes advanced are the lethargy and anorexia which are common symptoms of advanced renal disease. If clinically it can be observed that there is a relatively greater reduction in body weight than height, this possibility is more tenable. It is postulated by many that the effect of malnourishment is mediated through reduction of pituitary function, with decrease of somatotropin elaboration. This is purely speculative. Selye[2] has previously pointed out, however, that stress in general tends to increase the output of ACTH and decrease the output of growth hormone, both factors tending to result in stunted growth.

Chronic acidosis is the second most important cause for the growth failure of renal disease, and is found in about 70 per cent of all cases of renal growth failure. Conversely, all patients with chronic renal acidosis fall below the tenth percentile for height and weight. In a typical patient with renal disease, growth virtually stops at the time of onset of the renal acidosis. After a period of time, usually measured in years, the patient may again begin to grow despite the acidosis; this probably occurs through some as yet unexplained compensatory mechanism. There are several explanations of the inhibition of growth due to acidosis. There is, of course, the altered distribution of electrolytes with probable interference with normal cellular metabolism. There is also a compensatory reduction of the gastric acidity with a resultant decreased calcium absorption. Finally, phosphate retention tends to cause depression of serum calcium with secondary bone resorption. Such changes in bone are rarely demonstrated roentgenographically due to the fact that as much as 30 per cent of the osseous calcium must be removed before x-ray changes may be noted. Azotemia was found in 81 per cent of our cases of renal growth failure. However, many patients with mild nitrogen retention, in the absence of a renal defect, had normal growth. No one has ever demonstrated a true toxic effect of a high blood urea nitrogen. It is possible that, along with the nitrogen retention, other catabolic substances are also retained, although none has as yet been demonstrated.

Proteinuria might also logically seem to result in negative nitrogen balance. It is interesting therefore, that almost all children with lipoid

nephrosis, even in the face of gross albuminuria, attain normal height and weight in the absence of edema.

We have recently treated a premature infant at our hospital. This child was the result of a normal gestation and delivery and weighed 3 pounds 4 ounces at birth. He was transferred to our hospital at age 8 days for routine care, and at this time an abdominal mass was palpated. Urological studies were performed and revealed a total lack of function of the left kidney; this was later found to be due to a complete atresia of the left ureter. In addition, bilateral cystic kidneys were found, and there was marked hydronephrosis on the right side. The infant had a left nephrectomy and a right pyelostomy. Despite this, the child's growth was fairly normal following a slight fall-off shortly after surgery. At this time the child's blood urea nitrogen was in a range of 70 to 80 mg. per 100 ml. and the urine concentrated at best to 1.010. His subsequent growth during a period of a year, despite a persistently high blood urea nitrogen and a persistent inability to concentrate urine, was very good, indicating that decreased concentrating ability and retention of nitrogen, in themselves, perhaps play no great role in growth failure.

It is not known for certain why the presence of renal excretory failure should lead to the development of gross skeletal abnormalities. Lucas,[3] in 1883, first recorded rickets in renal disease and gave it its name. Conflicting theories have been presented as to the actual pathologic changes, and in 1948, Albright and Reifenstein[4] stated that renal rickets was actually synonymous with renal osteitis fibrosa cystica. However, many investigators before and since have demonstrated that the lesions of osteomalacia are also present in these patients. Disturbances of all biological processes involving bone may be detected in renal rickets secondary to marked renal acidosis. Children, in general, tend to live longer with chronic renal disease than do adults, and this perhaps accounts for the more frequent involvement of bones in children.

There is an almost complete lack of bone growth once the onset of renal rickets has occurred. Arrest of endochrondral growth at the epiphyses may result in typical dwarfism. Typical rachitic changes may be noted at the ends of the long bones. Failure of integrated processes for remodeling of the long bones results in abnormal stress lines and weaker structure. Stimulation of the absorption of calcium from bone by chronic acidosis or secondary hyperparathyroidism results in replacement of the trabeculae by fibrous tissue with a resultant reduction in skeletal density.

The removal of calcium may also result in cyst formation, giving rise to the typical cysts of osteitis fibrosa cystica. There also may be reactive bone formation with the deposition of bone either beneath the periostium or in other soft tissue structures.

It is therefore not possible to describe renal osteodystrophy as a simple or single pathological entity. The many components in the skeletal spectrum, i.e., rickets or osteomalacia, osteitis fibrosa cystica, and osteosclerosis, invite further investigation because of their relevance to the general problem of metabolic bone disease. A possible pathophysiological explanation of bone changes in chronic renal acidosis is suggested by the inability of the kidney to excrete phosphorus which results in an increased fecal excretion of phosphorus, with the result that ingested calcium is bound to the phosphates in the bowel, and a decreased absorption of calcium occurs. Thus, a true rachitic type of bone change is found. Many authors feel that chronic renal disease leads to an acquired insensitivity to vitamin D; proof of this, however, is completely lacking.

Most American authors feel that osteomalacia is a relatively unimportant part of the bone pathology and point to the more distinctive changes of cyst formation, decreased bone density, wooly appearance of the epiphyses, the presence of asymmetrical lesions, and metastatic calcifications, all indications of osteitis fibrosa cystica. Whether these lesions of bone absorption result from acidosis alone or are the result of secondary hyperparathyroidism in response to low blood calcium has not been established. Hormone assay studies have been equivocal. At autopsy, parathyroid hyperplasia with chief cell proliferation is a common finding. Gilmour,[5] in 1947, suggested that the parathyroid weight was roughly proportional to the amount of osteitis fibrosa cystica present.

Treatment of true rachitic bone disease consists of carefully controlled administration of very large doses of vitamin D. Occasionally, even the lesions of osteitis fibrosa cystica seem to respond to this treatment. However, if the primary lesion is osteitis fibrosa cystica, and particularly if metastatic calcification is present, such vitamin D therapy is contraindicated because of possible abnormal deposition of calcium. Of even more significance is the possibility of nephrocalcinosis with increased renal impairment.

There remain the hereditary diseases of impaired tubular dysfunction. These include the so-called phosphate diabetes or de Toni-Fanconi syndrome, cystinosis, and the Lightwood-Albright syndrome. From the point of view of rachitic changes, two types are definable: first, those lesions of the proximal tubules with loss of amino acids, glucose and phosphate, which result in rachitic changes due to low blood phosphates, and second, lesions of the distal tubules with the inability to form ammonia and an acid urine, with the resultant loss of base including calcium. In renal tubular disease, the changes are those of true rickets and are exactly similar to those found in vitamin D insufficiency.

REFERENCES

1. West, C. D., and Smith, W. C.: An attempt to elucidate the cause of growth retardation in renal disease, A.M.A. Am. J. Dis. Child. **91**: 460, 1956.
2. Selye, H.: The Physiology and Pathology of Exposure to Stress: A Treatise Based on the Concepts of the General-Adaptation-Syndrome and the Diseases of Adaptation, Montreal, Canada, Acta, Inc., 1950.
3. Lucas, R. C.: referred to in Stanbury, S. W.: Azotaemic renal osteodystrophy, Brit. M. Bull. **13**: 57, 1957.
4. Albright, F., and Reifenstein, E. C. Jr.: The Parathyroid Glands and Metabolic Bone Disease: Selected Studies, Baltimore, The Williams & Wilkins Company, 1948.
5. Gilmour, J. R.: The Parathyroid Glands and Skeleton in Renal Disease, Oxford University Press, New York & London, 1947.

The Role of Infection in Growth Failure

Lieutenant R. Miller, Jr., MC, U.S.N.

It is evident that for proper growth, both skeletal tissue and soft tissues must be able to respond to appropriate stimuli in the presence of certain anabolic hormones. Equally important is adequate nutrition for the maintenance of positive nitrogen balance, and quite obviously, properly functioning processes to ensure the utilization of nutritional substances.

Evidence pertaining to the effect of infections upon growth is rather nebulous. Available data, for the most part, represent qualitative impressions. However, it does appear that infection can affect statural growth, and this effect may be either local or general in nature. Destructive vertebral lesions with secondary collapse and wedging can mechanically reduce height. In an entirely opposite sense, local infection can increase bone length; this is seen with the metaphysial neovascularization occurring in osteomyelitis.

In the case of acute infection, it appears that there is a compensatory mechanism which permits growth to resume its constitutional or intrinsic pattern during the phase of recovery. Apart from the obvious effects of anorexia and fever, the deceleration or arrest in growth that occurs with infection is unexplained. It may well be that bed rest and the associated negative nitrogen balance are contributory.

The most extreme examples of growth retardation are met with in areas where helminthiasis, such as hookworm and tapeworm infestations, exists, or in tropical countries where diseases such as malaria are endemic. Is it

possible to postulate any pathophysiological mechanism to explain, for example, the growth retardation that occurs in hookworm disease? Experimentally, it can be shown that animals that are rendered both anemic and hypoproteinemic will preferentially utilize dietary protein for the formation of hemoglobin rather than for the reconstitution of body mass, and, presumably, skeletal development.

There are very few quantitative studies relating to the effect of childhood disease on skeletal development. One of the most recent and perhaps the very best, was carried out by the Social Medicine Unit at Oxford University. This study involved 650 individual children during what would represent more than 2,000 child years of observation. Diseases suffered by these youngsters included measles, chicken-pox, rubella, scarlet fever, pertussis, mumps, otitis media, mastoiditis, laryngitis, bronchitis, pneumonia, skin infections such as impetigo, scabies, and eczema, and a host of other minor infections which were mostly intestinal in nature. The final statistical evaluation showed that there was indeed a stunting effect when the heights of a group of children who had been ill in any given year were compared with a similar group who had remained healthy. However, in absolute terms, this stunting effect amounted to rather less than one quarter of an inch and it was in fact tiny when compared with the natural variation in the height of the children. From these data, it is not unreasonable to conclude that since most diseases are of short duration, and since there does appear to be a compensatory mechanism allowing for acceleration of growth during convalescence, the transitory effects of most illnesses and perhaps even an occasional more prolonged and severe one are clinically unrecognizable.

Closing Comments

CAPTAIN CONE

One last thing that concerns many parents who have school-age children is that the desks for the second grade children are no longer adequate for second grade children. Actually, the second grade children fit into the third or fourth grade classrooms, and the fourth grade children belong in the fifth or sixth grade classrooms. Standards of desk and classroom size established by construction companies a generation or two ago were wonderful, but our children just don't fit these standards anymore because of a tremendous secular acceleration of growth. Clements,[1] in 1953, has

shown that the trend over a seven year interval in England was that the 6 year old in 1953 was equivalent in height and weight to the 8½ to 9 year old in 1883. This can be matched easily in this country. How do we explain this? A variety of explanations have been offered but no one explanation holds. Most students of the secular trend have regarded it as the net expression of forces, including availability of food, a better understanding of nutrition, relative freedom from serious and prolonged illnesses, better family units, and public sanitation. Nevertheless, the paradox remains that as each single item is individually tested for significance by careful matching of samples, as the data and changing conditions of the times permit, a large section of growth acceleration remains unexplained. This promises an extremely promising assignment for future study.

This tremendous growth acceleration applies not only to velocity of growth but also to maturation. Dr. Tanner in his book, "Growth at Adolescence"[2] has a chart to show that the menarche in Norway in 1850 occurred sometime between the seventeenth and the seventeenth and a half year. The curves of age of onset of menstruation are downward for any country observed, particularly in the western world. Our American girls are menstruating much earlier than those a generation ago. This is a straight line curve and how long this will continue, no one can tell; perhaps, the rapidity of maturation, or the earlier maturation results in a biologic age far different from what we consider the chronologic capabilities of these children. This may explain the reason for early dating, "going steady," and dancing in the seventh grade in junior high school. Parents almost always state, "We never did that when we were in the seventh grade." But, if we were to look at pictures of ourselves when we graduated from elementary school, it is easy to see that we looked like children, and we were. Now, children at the eighth grade or junior high school level, are biologically far more advanced. This brings up all sorts of social problems because in the past era the menstrual period was an indication of biologic maturation, and if it occurred at 16, 16½, or 17 years of age, marriage was not far off. But now, many girls menstruate at 10½ to 11 years of age, and with a much more prolonged educational exposure and perhaps not being able to marry until they are 20 or 21, many will develop all sorts of psychosexual difficulties. This perhaps explains some of the tensions we, as parents, have with our growing teen-agers.

REFERENCES

1. Clements, E. M. B.: Changes in mean stature and weight of British children over the past 70 years, Brit. M. J. **2**: 897, 1953.
2. Tanner, J. M.: Growth at Adolescence, Springfield, Illinois, Charles C Thomas, 1955, p. 93.

The Editor's Column

TEAMWORK

As medical skill and knowledge increase, there is a trend among physicians toward more selective specialization. Because of his limited focus, the superspecialist is often unable to view all the aspects of the patient and his problems. Other specialists must then be called upon to handle other facets of the patient or his illness, and the complexities of care multiply. In order to avoid this compartmental outlook, teams of specialized medical and ancillary personnel have been organized to care for children with complex illnesses such as poliomyelitis, cerebral palsy, cleft palate, and congenital heart disease. The comprehensive care offered by teams of surgeons, pediatricians, psychiatrists, physical therapists, social workers, etc., no matter how effective, does not include the day to day care and individual interest that is expected from a personal physician.

If this personal touch is not to become a remnant of the "good old days" of inadequate care and incomplete knowledge, the child's family doctor must be kept informed by the team of the child's status and progress under their care. Then the team approach can be coordinated with the day by day routine as outlined by the family physician. In addition, the child's doctor must keep himself generally informed about his patient's disease, so that he may better interpret to the parents the work of the team.

On a smaller scale, this same teamwork is essential in private consultations. If the referring physician cannot be present with the consultant, it behooves him to inform the consultant of the reason for seeking his opinion. Discussion by the two physicians of the consultant's findings and recommendations is imperative, so that the parents will not be confused by conflicting reports. There should be no question in the minds of any of the parties as to which physician is responsible for continuation of the patient's care.

Finally, the child and his parents must be considered as members as well as beneficiaries of the team. In an era when lay people show increasing interest in and awareness of medical matters, they can be expected to ask pertinent questions and to resent impertinent replies. They are entitled to know not only what is in store for their child, but also how and why. When the child and parent are consulted in the planning of the program of therapy, they are more likely to cooperate, and the professional members of the team will realize better results.

In our attempts at perfection in medical care, we must not overlook the tremendous importance of mutual respect and cooperation between the specialized members of the team, the family physician, and the family.

G. J. C

Only the label tells you the B-vitamins are present

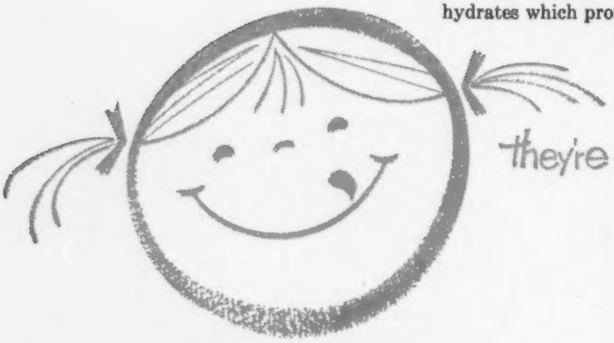
new, improved Poly-Vi-Sol® tablets

6 essential vitamins, Mead Johnson

first vitamin product ever with tasteless B

She's eager for vitamin time because the typical B-vitamin taste and odor have been masked.

- Improved formulation—20% more vitamin C and more B-complex, too.
- Now adequate for children of all ages.
- Delicious, and do not contain carbohydrates which promote dental caries.



they're chewable!

Mead Johnson
Symbol of service in medicine

ent

!